

Claims

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1. A stable non-aqueous single phase biocompatible viscous vehicle capable of suspending beneficial agents and homogeneously dispensing said beneficial agent over an extended period of time at body temperature and at low flow rates.
2. The vehicle of claim 1 comprising two components selected from the group consisting of solvent, surfactant, and polymer, wherein the two components are not of the same type.
3. The vehicle of claim 1 comprising at least two components selected from the group consisting of solvent, surfactant, and polymer, wherein the components are not of the same type.
4. The vehicle of claim 1 which comprises three components selected from the group consisting of solvent, surfactant, and polymer, wherein the components are not of the same type.
5. The vehicle of claim 2 or 4 wherein said solvent is selected from the group carboxylic acid esters, polyhydric alcohols, polymers of polyhydric alcohols, fatty acids, oils, propylene carbonate, lauryl alcohol, and esters of polyhydric alcohols.
6. The vehicle of claim 2 or 4 wherein said surfactant is selected from the group esters of polyhydric alcohols, ethoxylated castor oil, polysorbates, esters or ethers of saturated alcohols, and polyoxyethylenepolyoxypropylene block copolymers.
7. The vehicle of claim 2 or 4 wherein said polymer is selected from the group polyesters, pyrrolidones, esters or ethers of unsaturated alcohols, and polyoxyethylenepolyoxypropylene block copolymers.

8. The vehicle of claim 2 wherein the ratios of the components are in the range of 40:60 to 60:40.

9. The vehicle of claim 4 wherein the ratios of the components are in the 5 range of about 30% to about 50% for solvent, about 5% to about 20% for surfactant, and about 5% to about 60% for polymer.

10. The vehicle of claim 4 wherein the polymer is polyvinylpyrrolidone, the surfactant is gml, and the solvent is lauryl lactate.

11. The vehicle of claim 4 wherein the polymer is polyvinylpyrrolidone, the surfactant is polysorbate, and the solvent is lauryl lactate.

12. The vehicle of claim 1 which comprises an antioxidant.

13. The vehicle of claim 12 wherein said antioxidant is selected from the group consisting of tocopherol, ascorbic acid, ascorbyl palmitate, butylated hydroxyanisole, butylated hydroxytoluene, and propyl gallate.

20 14. A stable non-aqueous viscous protein formulation comprising
a) at least one beneficial agent, and
b) a non-aqueous single phase biocompatible viscous vehicle, which formulation is capable of being uniformly dispensed over an extended period of time at a low flow rate.

25 15. A non-aqueous formulation comprising at least one beneficial agent uniformly suspended in a non-aqueous single phase biocompatible viscous vehicle, which formulation can be delivered from an implantable drug delivery system such that the exit shear rate of the formulation is between about 1 and 30 1×10^{-7} reciprocal second.

16. The formulation of claim 14 wherein said formulation is stable at body temperature for extended periods of time.

17. The formulation of claim 14 which comprises at least about 0.1% (w/w) beneficial agent.

5 18. The formulation of claim 14 which comprises at least about 10% (w/w) beneficial agent.

10 19. The formulation of claim 14 wherein said beneficial agent is selected from the group consisting of peptide, protein, nucleotide, hormone, virus, or antibody.

15 20. The formulation of claim 19 wherein said beneficial agent is a protein.

21. The formulation of claim 14 which is stable at 65° C for at least about 2 months.

15 22. The formulation of claim 14 which is stable at 37° C for at least about 3 months.

20 23. The formulation of claim 14 which is stable at 37° C for at least about one year.

25 24. The formulation of claim 14 which is adapted for use in an implantable drug delivery device.

25 25. The formulation of claim 14 wherein said vehicle is selected from the group consisting of solvent, surfactant and polymer.

30 26. The formulation of claim 14 wherein said vehicle comprises an antioxidant.

27. The formulation of claim 14 comprising a beneficial agent which has been dried to a low moisture content prior to incorporation in said formulation.

28. The formulation of claim 14 which is stable after sterilization.

29. A method for preparing the stable single phase viscous vehicle of claim 1 comprising the steps of (1) blending the ingredients at elevated temperature under dry conditions to allow them to liquify, and (2) allowing the liquid from step (1) to cool to room temperature.

30. A method for preparing the stable formulation of claim 14 comprising combining the single phase viscous vehicle and beneficial agent under dry conditions and blending them under vacuum at elevated temperature to uniformly disperse the beneficial agent in the vehicle, and allowing the formulation to cool to room temperature.

31. The method of claim 30 wherein at least about 0.1% (w/w) beneficial agent is suspended in said vehicle.

32. The method of claim 30 wherein at least about 10% (w/w) beneficial agent is suspended in said vehicle.

33. A method for treating a subject suffering from a condition which may be alleviated by administration of a beneficial agent comprising administering to said subject a therapeutically effective amount of the formulation of Claim 14.

34. The method of claim 33 wherein said administration is parenteral administration.

35. The method of claim 33 wherein said administration is long-term continuous administration.

36. The method of claim 33 wherein said administration is accomplished by use of an implantable drug delivery system.

37. The method of claim 33 wherein said daily administration continues for a period selected from the group consisting of about 3 months, about 6 months, and about 12 months.

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38. The method of claim 37 wherein said daily administration is accomplished using an implantable drug delivery system.

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